Mathematical analysis of stochastic models for tumor-immune systems

O. Chiş*, D. Opriş**

* Euro University "Drăgan", Lugoj, Romania
** Faculty of Mathematics and Informatics, West University of Timişoara, Romania
E-mail: chisoana@yahoo.com, opris@math.uvt.ro

Abstract: In this paper we investigate some stochastic models for tumor-immune systems. To describe these models we used a Wiener process, as the noise has a stabilization effect. Their dynamics are studied in terms of stochastic stability in the equilibrium points, by constructing the Lyapunov exponent, depending on the parameters that describe the model. We have studied and analyzed a Kuznetsov-Taylor like stochastic model and a Bell stochastic model for tumor-immune systems. These stochastic models are studied from stability point of view and they were represented using the Euler second order scheme.

MSC2000: 37L55, 65C30, 37H15, 60H20, 76M35.

Keywords: stochastic model, stochastic stability, Wiener process, Lyapunov exponent, tumor-immune systems, Euler second order scheme.

1 Introduction

Cancer is a disease that may affect people at all ages. It causes about 13% of all human deaths. In the prognosis of cancer patients, it should be taken into consideration the type of cancer and the stage of the disease. Cancers may be treated or cured, depending on the specific type, location, and stage. We may say that surgery and chemotherapies play an important role in treating cancer, but they do not represent a cure. What it is needed is a successful treatment strategies, one of these strategies is investigated through immunotherapy [13], by defining a model of differential equations that represents the interaction

between effector cells and tumor cells. This idea of immunotherapy is promising, but controversial from the point of view of the results obtained in medical investigations.

Stochastic modelling plays an important role in many branches of science. Because in practical situations we confront with instability and perturbations, we will express our mathematical models using white noise, represented by brownian motion. We will study stochastic dynamical systems that are used in medicine, in describing a tumor behavior. Cancer tumor may be destroyed using some treatments, but a regression of the disease may appear. So, we need not only preventative measures, but also more successful treatment strategies. Efforts along these lines are now being investigated through immunotherapy ([5], [20], [22]). A simulating model is described by the existence of tumor free equilibrium. A tumor size may tend to $+\infty$, depending on the parameters of the model, and may exist a "small tumor size" equilibrium, which coexists with the tumor free equilibrium [10].

This tumor-immune study, from theoretical point of view, has been done for two cell populations: effector cells and tumor cells. It was predicted a threshold above which there is uncontrollable tumor growth, and below which the disease is attenuated with periodic exacerbations occurring every 3-4 months. There was also shown that the model does have stable spirals, but the Dulac-Bendixson criterion demonstrates that there are no stable closed orbits. It is consider ODE's for the populations of immune and tumor cells and it is shown that survival increases if the immune system is stimulated, but in some cases an increase in effector cells increases the chance of tumor survival.

In the last years, stochastic growth models for cancer cells were developed. These models simulate the way tumors evolve with respect to a certain therapy, but also they show the interactions between tumor cells and immune cells. We mention the papers of W.Y. Tan and C.W. Chen [19], N. Komarova, G. Albano and V.Giorno [1], L. Ferrante, S. Bompadre, L. Possati and L. Leone [6], A. Boondirek Y. Lenbury, J. Wong-Ekkabut, W. Triampo, I.M. Tang, P. Picha [4].

Our goal in this paper is to construct stochastic models and to analyze their behavior around the equilibrium point. In these points stability is studied by analyzing the Lyapunov exponent, depending of the parameters of the models. Numerical simulations are done using a deterministic algorithm with an ergodic invariant measure. In this paper, the authors studied and analyzed two stochastic models. In Section 2, we considered a Kuznetsov and Taylor stochastic model. Beginning from the classical one, we have studied the case of positive immune response. We gave the stochastic model and we analyzed

it in the equilibrium points. Numerical simulations for this new model are presented in Section 2.1. In Section 3 we presented a general family of tumor-immune stochastic systems and from this general representation, we analyzed Bell model. We wrote this model as a stochastic model, using Annexe 1, and we discussed its behavior around the equilibrium points. Numerical simulations were done using the software Maple 12 and we implemented the second order Euler scheme for a representation of the discussed stochastic models, described in Annexe 2.

2 Kuznetsov and Taylor stochastic model

We will begin our study from the model of Kuznetsov and Taylor [13]. This model describes the response of effector cells to the growth of tumor cells and takes into consideration the penetration of tumor cells by effector cells, that causes the interaction of effector cells. This model can be represented in the following way:

$$\begin{cases} \dot{x}(t) = a_1 - a_2 x(t) + a_3 x(t)y(t), \\ \dot{y}(t) = b_1 y(t)(1 - b_2 y(t)) - x(t)y(t), \end{cases} \tag{1}$$

where initial conditions are $x(0) = x_0 > 0$, $y(0) = y_0 > 0$ and a_3 is the immune response to the appearance of the tumor cells.

In this paper we consider the case of $a_3 > 0$, that means that immune response is positive. For the equilibrium states P_1 and P_2, we study the asymptotic behavior with respect to the parameter a_1 in (1). For $b_1 a_2 < a_1$, the system (1) has the equilibrium states $P_1(x_1, y_1)$ and $P_2(x_2, y_2)$, with

$$x_1 = \frac{a_1}{a_2},\ y_1 = 0, \tag{2}$$

$$x_2 = (b_1(a_3 - b_2 a_2) + \sqrt{\Delta})/(2a_3),\ y_2 = (b_1(a_3 + b_2 a_2) - \sqrt{\Delta}/(2b_1 b_2 a_3) \tag{3}$$

where $\Delta = b_1^2(b_2 a_2 - a_3)^2 + 4b_1 b_2 a_1 a_3$.

In [13] it is shown that there is an a_{10} such that if $a_1 < a_{10}$, the equilibrium state P_1 is asymptotical stable, for $a_1 > a_{10}$ the equilibrium state P_1 is unstable and if $a_1 < a_{10}$ the equilibrium state P_2 is unstable and for $a_1 > a_{10}$ the equilibrium state P_2 is asymptotical stable.

In the following, we associate a stochastic system of differential equations to the classical system of differential equations (1).

Let us consider $(\Omega, \mathcal{F}_{t\geq 0}, \mathcal{P})$ a filtered probability space and $(W(t))_{t\geq 0}$ a standard Wiener process adapted to the filtration $(\mathcal{F})_{t\geq 0}$. Let $\{X(t) = (x(t), y(t))\}_{t\geq 0}$ be a stochastic process.

The system of Itô equations associated to system (1) is given by

$$\begin{aligned} x(t) &= x_0 + \int_0^t (a_1 - a_2 x(s) + a_3 x(s)y(s))ds + \int_0^t g_1(x(s), y(s))dW(s), \\ y(t) &= y_0 + \int_0^t ((b_1 y(s)(1 - b_2 y(s)) - x(s)y(s))ds + \int_0^t g_2(x(s), y(s))dW(s), \end{aligned} \tag{4}$$

where the first integral is a Riemann integral, and the second one is an Itô integral. $\{W(t)\}_{t\geq 0}$ is a Wiener process [16].

The functions $g_1(x(t), y(t))$ and $g_2(x(t), y(t))$ are given in the case when we are working in the equilibrium state. In P_1 those functions have the following form

$$\begin{aligned} g_1(x(t), y(t)) &= b_{11}x(t) + b_{12}y(t) + c_{11}, \\ g_2(x(t), y(t)) &= b_{21}x(t) + b_{22}y(t) + c_{21}, \end{aligned} \tag{5}$$

where

$$c_{11} = -b_{11}x_1 - b_{12}y_1,\ c_{21} = -b_{21}x_1 - b_{22}y_1. \tag{6}$$

In the equilibrium state P_2, the functions $g_1(x(t), y(t))$ and $g_2(x(t), y(t))$ are given by

$$\begin{aligned} g_1(x(t), y(t)) &= b_{11}x(t) + b_{12}y(t) + c_{12}, \\ g_2(x(t), y(t)) &= b_{21}x(t) + b_{22}y(t) + c_{22}, \end{aligned} \tag{7}$$

where

$$c_{12} = -b_{11}x_2 - b_{12}y_2,\ c_{22} = -b_{21}x_2 - b_{22}y_2. \tag{8}$$

The functions $g_1(x(t), y(t))$ and $g_2(x(t), y(t))$ represent the volatilisations of the stochastic equations and they are the therapy test functions.

2.1 The analysis of SDE (4). Numerical simulation.

Using the formulae from Annexe 1, Annexe 2, and Maple 12 software, we get the following results, illustrated in the figures below. For numerical simulations, we use the following values for the parameters of the system (4):

$$a_1 = 0.1181,\ a_2 = 0.3747,\ a_3 = 0.01184,\ b_1 = 1.636,\ b_2 = 0.002.$$

The matrices A and B are given, in the equilibrium point $P_1(\frac{a_1}{a_2}, 0)$ by

$$A = \begin{pmatrix} -a_2 + a_3 y_1 & a_3 x_1 \\ -y_1 & b_1 - 2b_2 y_1 - x_1 \end{pmatrix}, \quad B = \begin{pmatrix} 10 & -2 \\ 2 & 10 \end{pmatrix}.$$

In a similar way, matrices A and B are defined in the other equilibrium point

$$P_2\Big(\frac{(-b_1(b_2a_2 - a_3) + \sqrt{\Delta})}{2a_3}, \frac{(b_1(b_2a_2 + a_3) - \sqrt{\Delta})}{2b_1b_2a_3}\Big),$$

with $\Delta = b_1^2(b_2a_2 - a_3)^2 + 4b_1b_2a_1a_3$.

Using the second order Euler scheme for the ODE system (1), respectively SDE system (4), we get the following orbits.

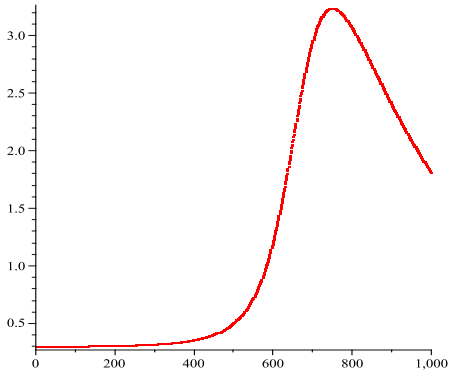

Fig 1: $(n, x(n))$ in P_1 for ODE (1)
optimal behavior of tumor cells
for ODE(1) in P_1

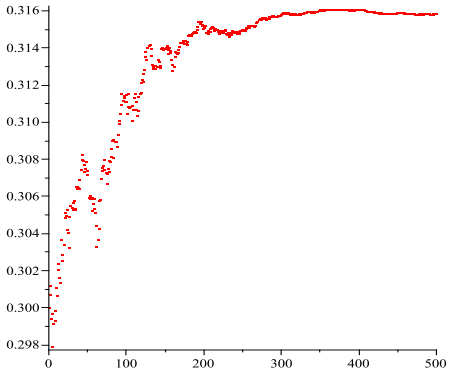

Fig 2: $(n, x(n, \omega))$ in P_1 for SDE (4)
optimal behavior of tumor cells
for ODE(4) in P_1

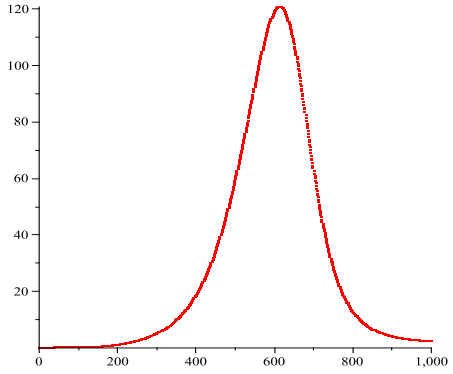

Fig 3: $(n, y(n))$ in P_1 for ODE (1)
optimal behavior of effector cells for
for ODE(1) in P_1

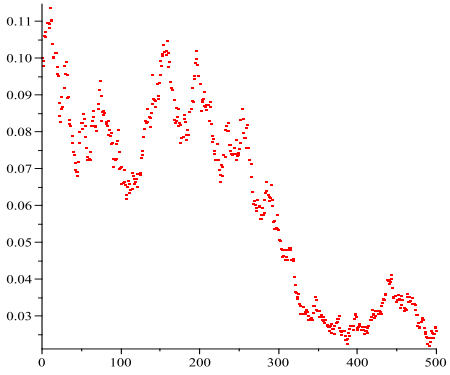

Fig 4: $(n, y(n, \omega))$ in P_1 for SDE (4)
optimal behavior of effector cells
for ODE(4) in P_1

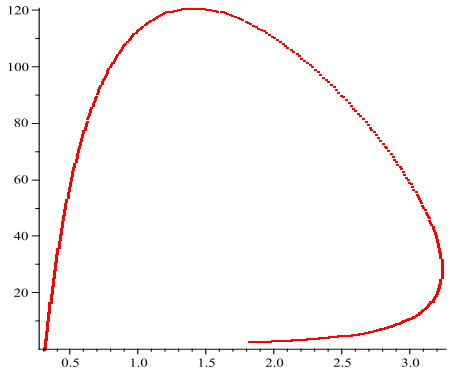

Fig 5: $(x(n), y(n))$ in P_1 for ODE (1)
optimal behavior of tumor cells
vs effector cells for ODE(1) in P_1

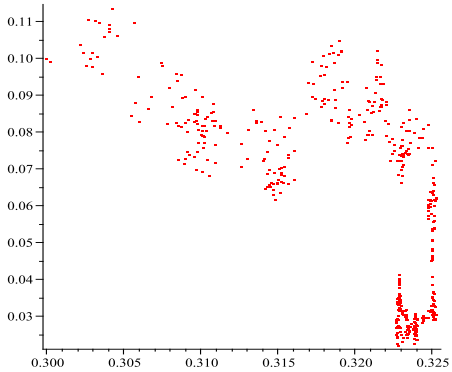

Fig 6: $(x(n,\omega), y(n,\omega))$ in P_1 for SDE (4)
optimal behavior of tumor cells
vs effector cells for ODE(4) in P_1

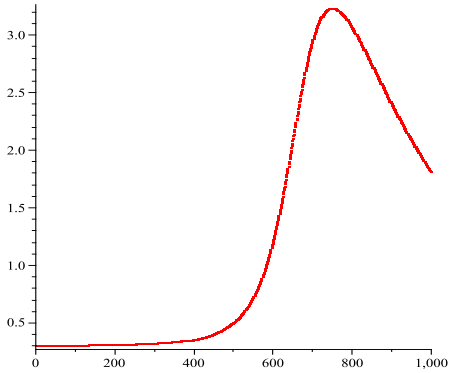

Fig 7: $(n, x(n))$ in P_2
optimal behavior of tumor cells
for ODE(1) in P_2

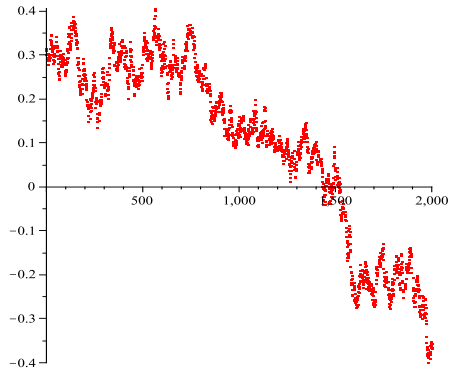

Fig 8: $(n, x(n,\omega))$ in P_2
optimal behavior of tumor cells
for ODE(4) in P_2

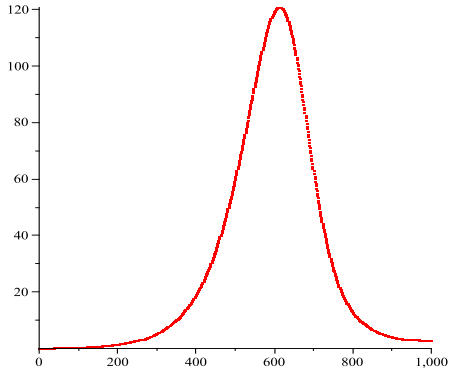

Fig 9: $(n, y(n))$ in P_2
optimal behavior of effector cells
for ODE(1) in P_2

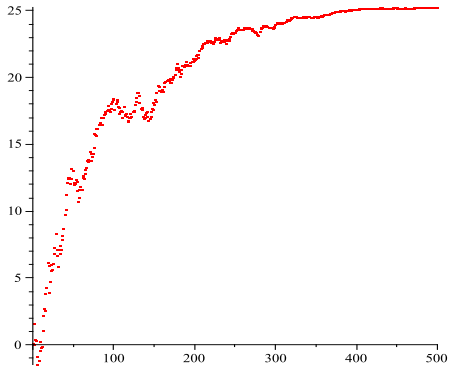

Fig 10: $(n, y(n,\omega))$ in P_2
optimal behavior of effector cells
for ODE(4) in P_2

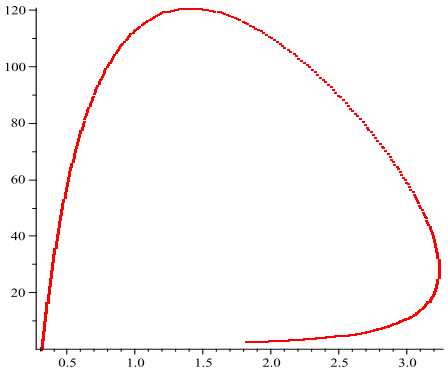

Fig 11: $(x(n), y(n))$ in P_2
optimal behavior of tumor cells
vs effector cells for ODE(1) in P_2

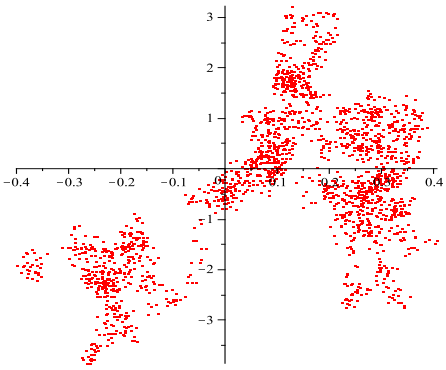

Fig 12: $(x(n,\omega), y(n,\omega))$ in P_2
optimal behavior of tumor cells
vs effector cells for ODE(4) in P_2

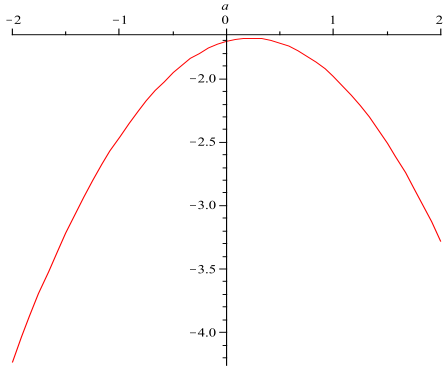

Fig 13: $(\alpha, \lambda(\alpha))$ in P_1

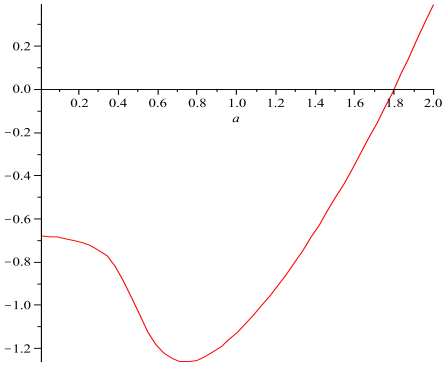

Fig 14: $(\alpha, \lambda(\alpha))$ in P_2

The Lyapunov exponent, for the equilibrium point P_1 is negative, so P_1 is asymptotically stable for each $\alpha \in \mathbb{R}$. For the equilibrium point P_2, it is asymptotically stable for all values of α from the interval $(-1.8, 1.8)$, that means that P_2 is unstable for all $\alpha \in (-\infty, -1.8) \cup (1.8, \infty)$.

3 A general family of tumor-immune stochastic systems

A Volterra-like model was proposed in [17], for the interaction between a population of tumor cells (whose number is denoted by x) and a population

of lymphocyte cells (y), and it is given by

$$\begin{cases} \dot{x}(t) = ax(t) - bx(t)y(t), \\ \dot{y}(t) = dx(t)y(t) - fy(t) - kx(t), \end{cases} \tag{9}$$

where the tumor cells are supposed to be in exponential growth (which is, however, a good approximation only for the initial phases of the growth) and the presence of tumor cells implies a decrease of the "input rate" of lymphocytes.

A general representation for such models can be considered in the form given by d'Onofrio in [5]:

$$\begin{cases} \dot{x}(t) = f_1(x(t), y(t)),\ \dot{y}(t) = f_2(x(t), y(t)), \\ x(0) = x_0,\ y(0) = y_0, \end{cases} \tag{10}$$

where x is the number of tumor cells, y the number of effector cells of immune system and

$$\begin{aligned} f_1(x(t), y(t)) &= x(t)(h_1(x(t)) - h_2(x(t))y(t)), \\ f_2(x(t), y(t)) &= (h_3(x(t)) - h_4(x(t)))y(t) + h_5(x(t)). \end{aligned} \tag{11}$$

The functions h_1, h_2, h_3, h_4, h_5 are given such that the system (10) admits the equilibrium points $P_1(x_1, y_1)$, with $x_1 = 0$, $y_1 > 0$, and $P_2(x_2, y_2)$, with $x_2 \neq 0$, $y_2 > 0$.

Particular cases, that will be discussed here, are the following:

Volterra model [21] if $h_1(x(t)) = a_1$, $h_2(x(t)) = a_2x(t)$, $h_3(x(t)) = b_3x(t)$, $h_4(x(t)) = b_2$ and $h_5(x(t)) = -b_1x(t)$;

Bell model [3] $h_1(x(t)) = a_1x(t)$, $h_2(x(t)) = a_2x(t)$, $h_3(x(t)) = b_1x(t)$, $h_4(x(t)) = b_3$ and $h_5(x(t)) = -b_2x(t) + b_4$;

Stepanova model [18] with $h_1(x(t)) = a_1$, $h_2(x(t)) = 1$, $h_3(x(t)) = b_1x(t)$, $h_4(x(t)) = b$ and $h_5(x(t)) = -b_2x(t) + b_4$;

Vladar-Gonzalez model [20] if in (10) we consider $h_1(x(t)) = \log(K/x(t))$, $h_2(x(t)) = 1$, $h_3(x(t)) = b_1x(t)$, $h_4(x(t)) = b_2 + b_3x^2(t)$ and $h_5(x(t)) = 1$;

Exponential model [22] if in (10) we consider $h_1(x(t)) = 1$, $h_2(x(t)) = 1$, $h_3(x(t)) = b_1x(t)$, $h_4(x(t)) = b_2 + b_3x^2(t)$, and $h_5(x(t)) = 1$;

Logistic model [14] if in (10) we consider $h_1(x(t)) = 1 - \frac{a_1}{x(t)}$, $h_2(x(t)) = 1$, $h_3(x(t)) = b_1x(t)$, $h_4(x(t)) = b_2 + b_3x^2(t)$, and $h_5(x(t)) = 1$.

For a considered filtered probability space $(\Omega, \mathcal{F}_{t\geq 0}, \mathcal{P})$ and a standard Wiener process $(W(t))_{t\geq 0}$, we consider the stochastic process in two dimensional space $(\mathcal{F})_{t\geq 0}$.

The system of Itô equations associated to system (10) is given, in the equilibrium point $P(x_0, y_0)$, by

$$\begin{aligned} x(t) &= x_0 + \int_0^t [x(s)(h_1(x(s)) - h_2(x(s))y(s)]ds + \int_0^t g_1(x(s), y(s))dW(s), \\ y(t) &= y_0 + \int_0^t [(h_3(x(s)) - h_4(x(s)))y(s) + h_5(x(s))]ds + \\ &\quad + \int_0^t g_2(x(s), y(s))dW(s), \end{aligned} \tag{12}$$

where the first integral is a Riemann integral, and the second one is an Itô integral. $\{W(t)\}_{t\geq 0}$ is a Wiener process [16].

The functions $g_1(x(t), y(t))$ and $g_2(x(t), y(t))$ are given in the case when we are working in the equilibrium state P_e, and they are given by

$$\begin{aligned} g_1(x(t), y(t)) &= b_{11}x(t) + b_{12}y(t) + c_{1e}, \\ g_2(x(t), y(t)) &= b_{21}x(t) + b_{22}y(t) + c_{2e}, \end{aligned} \tag{13}$$

where

$$c_{ie} = -b_{i1}x_e - b_{i2}y_e,\ i = 1, 2, \tag{14}$$

and $b_{ij} \in \mathbb{R}$, $i, j = 1, 2$.

3.1 Analysis of Bell model. Numerical simulations.

Following the algorithm for determining the Lyapunov exponent (A1) and the description of the second order Euler scheme (A2) in Maple 12 software, we get the following results, illustrated in the figures below. For numerical simulations we use the following values of parameters:

$$a_1 = 2.5,\ a_2 = 1,\ b_1 = 1,\ b_2 = 0.4,\ b_3 = 0.95,\ b_4 = 2.$$

The matrices A and B are given, in the equilibrium point P_1 by

$$A = \begin{pmatrix} -a_2y_1 + a_1 & -a_2x_1 \\ -b_2 + b_1y_1 & b_1x_1 - b_3 \end{pmatrix}, \quad B = \begin{pmatrix} \alpha & -\beta \\ \beta & \alpha \end{pmatrix},$$

with $\alpha = a \in \mathbb{R}$, $\beta = -2$. In a similar way the matrices A and B are defined in the equilibrium point $P_2\left(\frac{a_1b_3 - a_2b_4}{a_1b_1 - a_2b_2}, \frac{a_1}{a_2}\right)$.

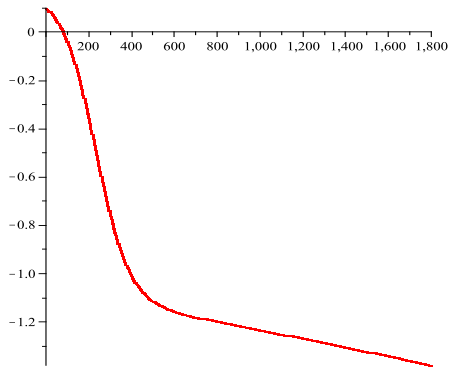

Fig 15: $(n, x(n))$ in P_1 for ODE (11)
optimal behavior of tumor cells
for ODE(11) in P_1

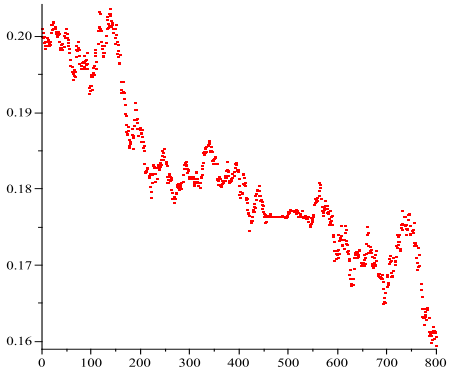

Fig 16: $(n, x(n, \omega))$ in P_1 for SDE (12)
optimal behavior of tumor cells
for ODE(12) in P_1

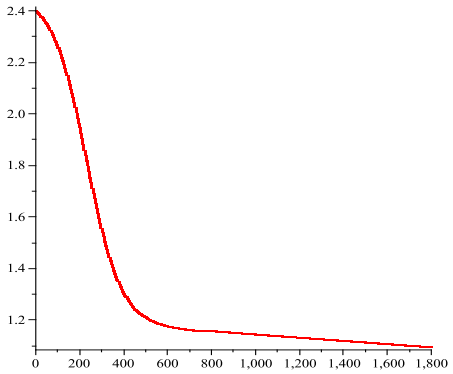

Fig 17: $(n, y(n))$ in P_1 for ODE (11)
optimal behavior of effector cells
for ODE(11) in P_1

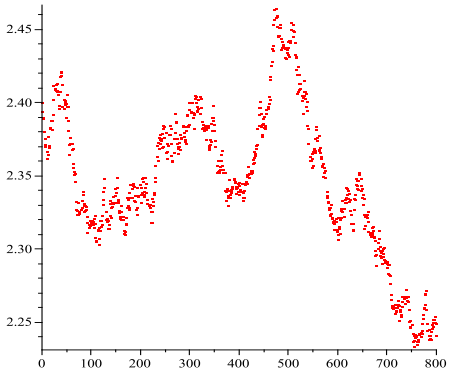

Fig 18: $(n, y(n, \omega))$ in P_1 for SDE (12)
optimal behavior of effector cells
for ODE(12) in P_1

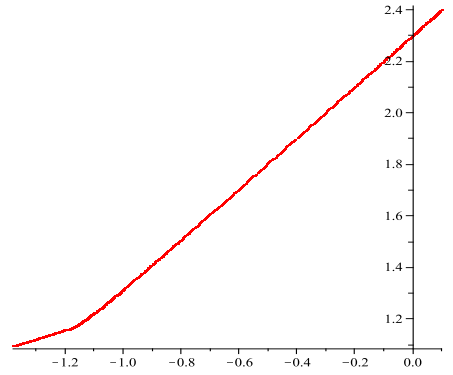

Fig 19: $(x(n), y(n))$ in P_1 for ODE (11)
optimal behavior of tumor cells
vs effector cells for ODE(11) in P_1

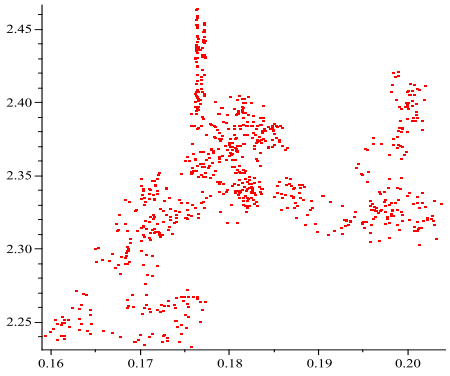

Fig 20: $(x(n, \omega), y(n, \omega))$ in P_1 for SDE (12)
optimal behavior of tumor cells
vs effector cells for ODE(12) in P_1

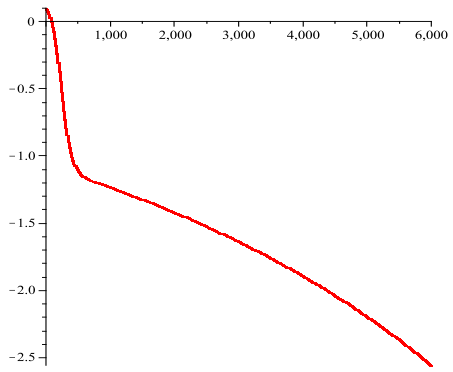

Fig 21: $(n, x(n))$ in P_2 for ODE (11)
optimal behavior of tumor cells
for ODE(11) in P_2

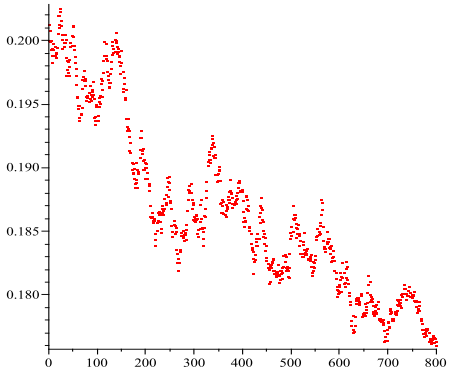

Fig 22: $(n, x(n, \omega))$ in P_2 for SDE (12)
optimal behavior of tumor cells
for ODE(12) in P_2

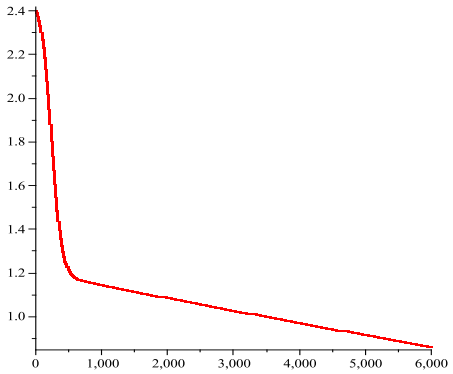

Fig 23: $(n, y(n))$ in P_2 for ODE (11)
optimal behavior of effector cells
for ODE(11) in P_2

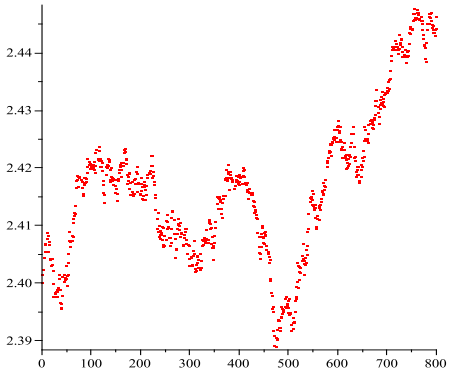

Fig 24: $(n, y(n, \omega))$ in P_2 for SDE (12)
optimal behavior of effector cells
for ODE(12) in P_2

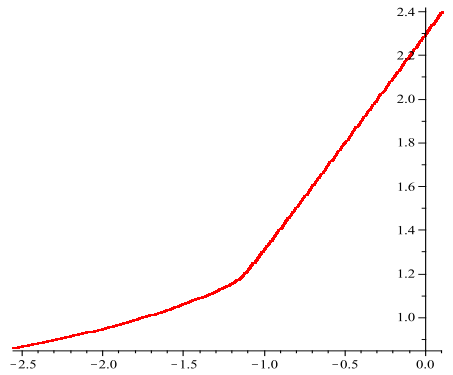

Fig 25: $(x(n), y(n))$ in P_2 for ODE (11)
optimal behavior of tumor cells
vs effector cells for ODE(11) in P_2

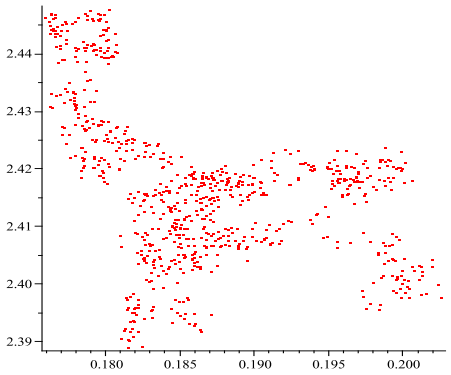

Fig 26: $(x(n, \omega), y(n, \omega))$ in P_2 for SDE (12)
optimal behavior of tumor cells
vs effector cells for ODE(12) in P_2

The Lyapunov exponent variation, with $b_{11} = \alpha$ a variable parameter, is given in Figure 27 for the equilibrium point P_1, and in Figure 28 for the equilibrium point P_2.

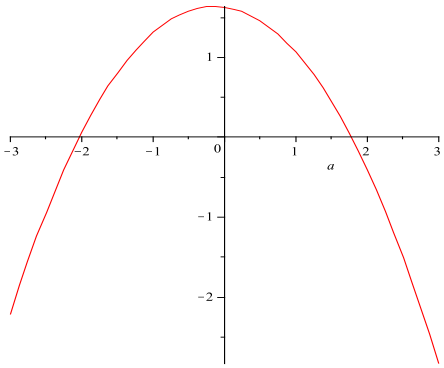

Fig 27: $(\alpha, \lambda(\alpha))$ in P_1

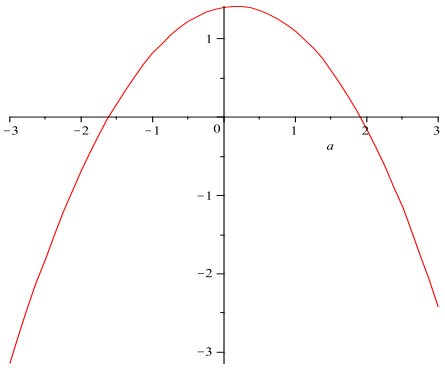

Fig 28: $(\alpha, \lambda(\alpha))$ in P_2

From the figures above, the equilibrium points P_1 and P_2 are asymptotically stable for all α such that the Lyapunov exponents $\lambda(\alpha) < 0$, and unstable otherwise. So, P_1 is asymptotically stable for $\alpha \in (-\infty, -1.78) \cup (2.02, \infty)$ and P_2 is asymptotically stable for $\alpha \in (-\infty, -1.62) \cup (1.88, \infty)$.

4 Conclusions

As considered in this paper, we used established conceptual models, but it is also very important to consider the model through all its aspects, as we have done in this case by imposing the positivity of its solutions. Even if the initial model violates the positivity rule, it is valuable because it may be read as a model which takes into account a disease-induced depression in the influx of lymphocytes. Then, instead of proposing another specific model, we preferred to add this new feature to a family of equations, and so, in particular to our models chosen for study.

We have focused on two important tumor-immune systems, presented from stochastic point of view: a Kuznetsov-Taylor model and Bell model, that belongs to a general family of tumor-immune stochastic systems. We have determined the equilibrium points and we have calculated the Lyapunov exponents. A computable algorithm is presented in A1. These exponents help us to decide whether the stochastic model is stable or not. For numerical simulations we

have used the Euler scheme presented in detail in A2 and the implementation of this algorithm was done in Maple 12. In a similar way other models given by (11) can be studied. The model given by the SDE (12) allows the control of the model given by ODE (1) with a stochastic process. This model is dependent on initial conditions. These are very difficult to find for a concrete case, that is why it is quite impossible to plan an anticancer therapy based only on this method. This is the ony disadvantage for the immunotherapy.

In our further work, we will consider the tumor-immune model with delay, and also another technique used for a successful therapy, using synchronization of the coupled tumor-immune model of repressilators in tumor cells aggregations.

Annexe

A1 Lyapunov exponents and stability in stochastic 2-dimensional structures.

The behavior of a deterministic dynamical system which is disturbed by noise may be modelled by a stochastic differential equation (SDE). In many practical situations, perturbations are generated by wind, rough surfaces or turbulent layers are expressed in terms of white noise, modelled by brownian motion. The stochastic stability has been introduced by Bertram and Sarachik [12] and is characterized by the negativeness of Lyapunov exponents. But it is not possible to determine this exponents explicitly. Many numerical approaches have been proposed, which generally used simulations of stochastic trajectories.

Let $(\Omega, \mathcal{F}, \mathcal{P})$ a probability space. It is assumed that the $\sigma-$algebra $\mathcal{F}_t (t \geq 0)$ such that

$$\mathcal{F}_s \subset \mathcal{F}_t \subset \mathcal{F}, \forall\, s \leq t,\ s, t \in I,$$

where $I = [0, T]$, $T \in (0, \infty)$.

Let $\{x(t) = (x_1(t), x_2(t))\}_{t \geq 0}$ be a stochastic process. The system of Itô equations

$$dx_i(t, \omega) = f_i(x(t, \omega))dt + g_i(x(t, \omega))dW(t, \omega),\ i = 1, 2, \tag{15}$$

with initial condition $x(0) = x_0$ is interpreted in the sense that

$$x_i(t, \omega) = x_{i0}(t, \omega) + \int_0^t f_i(x(s, \omega))ds + \int_0^t g_i(x(s, \omega))dW(s, \omega),\ i = 1, 2, \tag{16}$$

for almost all $\omega \in \Omega$ and for each $t > 0$, where $f_i(x)$ is a drift function, $g_i(x)$ is a diffusion function, $\int_0^t f_i(x(s))ds$, $i = 1, 2$ is a Riemann integral and $\int_0^t g_i(x(s))dW(s)$, $i = 1, 2$ is an Itô integral. It is assumed that f_i and g_i, $i = 1, 2$ satisfy the conditions of existence of solutions for this SDE with initial conditions $x(0) = a_0 \in \mathbb{R}^n$.

Let $x_0 = (x_{01}, x_{02}) \in \mathbb{R}^2$ be a solution of the system

$$f_i(x_0) = 0,\ i = 1, 2. \tag{17}$$

The functions g_i are chosen such that

$$g_i(x_0) = 0,\ i = 1, 2.$$

In the following, we will consider

$$g_i(x) = \sum_{j=1}^{2} b_{ij}(x_j - x_{0j}),\ i = 1, 2, \tag{18}$$

where $b_{ij} \in \mathbb{R}$, $i = 1, 2$.

The liniarized of system (16) in x_0 is given by

$$X(t) = \int_0^t AX(s)ds + \int_0^t BX(s)dW(s), \tag{19}$$

where

$$X(t) = \begin{bmatrix} x(t,\omega) \\ y(t,\omega) \end{bmatrix}, \quad A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix}, \quad B = \begin{bmatrix} b_{11} & b_{12} \\ b_{21} & b_{22} \end{bmatrix} \tag{20}$$

$$a_{ij} = \frac{\partial f_i}{\partial x_j}\Big|_{x_0}, \quad b_{ij} = \frac{\partial g_i}{\partial x_j}\Big|_{x_0}. \tag{21}$$

The Oseledec multiplicative ergodic theorem [15] asserts the existence of two non-random Lyapunov exponents $\lambda_2 \leq \lambda_1 = \lambda$. The top Lyapunov exponent is given by

$$\lambda = \lim_{t\to\infty} \frac{1}{t} \sup \log \sqrt{x(t)^2 + y(t)^2}. \tag{22}$$

Applying the change of coordinates

$$x(t) = r(t)\cos\theta(t),\ x(t) = r(t)\sin\theta(t),$$

by writing the Itô formula for

$$h_1(x, y) = \frac{1}{2}\log(x^2 + y^2) = \log(r),$$

$$h_2(x, y) = \arctan\left(\frac{y}{x}\right),$$

results

Proposition 1

$$\log\Big(\frac{r(t)}{r(0)}\Big) = \int_0^t q_1(\theta(s)) + \frac{1}{2}(q_4(\theta(s))^2 - q_2(\theta(s))^2)ds + \int_0^t q_2(\theta(s))dW(s), \tag{23}$$

$$\theta(t) = \theta(0) + \int_0^t (q_3(\theta(s)) - q_2(\theta(s))q_4(\theta(s)))ds + \int_0^t q_4(\theta(s))dW(s), \tag{24}$$

where

$$\begin{array}{l} q_1(\theta) = a_{11}\cos^2\theta + (a_{12}+a_{21})\cos\theta\sin\theta + a_{22}\sin^2\theta, \\ q_2(\theta) = b_{11}\cos^2\theta + (b_{12}+b_{21})\cos\theta\sin\theta + b_{22}\sin^2\theta, \\ q_3(\theta) = a_{21}\cos^2\theta + (a_{22}-a_{11})\cos\theta\sin\theta - a_{12}\sin^2\theta, \\ q_4(\theta) = b_{21}\cos^2\theta + (b_{22}-b_{11})\cos\theta\sin\theta - b_{12}\sin^2\theta. \end{array} \tag{25}$$

As the expectation of the Itô stochastic integral is null,

$$E\int_0^t q_2(\theta(s))dW(s) = 0,$$

the Lyapunov exponent is given by

$$\lambda = \lim_{t\to\infty}\frac{1}{t}\log\Big(\frac{r(t)}{r(0)}\Big) = \lim_{t\to\infty}\frac{1}{t}E\int_0^t [q_1(\theta(s)) + \frac{1}{2}(q_4(\theta(s))^2 - q_2(\theta(s)))]ds.$$

Applying the Oseledec theorem, if $r(t)$ is ergodic, results that

$$\lambda = \int_0^t [q_1(\theta) + \frac{1}{2}(q_4(\theta)^2 - q_2(\theta))]p(\theta)d\theta, \tag{26}$$

where $p(\theta)$ is the probability distribution of the process θ. □

An approximation of this distribution is calculated by solving the Fokker-Planck equation. Associated with equation (24) for $p = p(t,\theta)$ we get

$$\frac{\partial p}{\partial t} + \frac{\partial}{\partial\theta}(q_3(\theta) - q_2(\theta)q_4(\theta)p) - \frac{1}{2}\frac{\partial^2}{\partial\theta^2}(q_4(\theta)^2 p) = 0. \tag{27}$$

From (27) results that the solution $p(\theta)$ of the Fokker-Planck equation is the solution of the following first order equation

$$(-q_3(\theta) + q_1(\theta)q_4(\theta) + q_2(\theta)q_5(\theta))p(\theta) + \frac{1}{2}q_4(\theta)^2 p'(\theta) = p_0, \tag{28}$$

where $p'(\theta) = \frac{dp}{d\theta}$ and

$$q_5(\theta) = -(b_{12}+b_{21})\sin 2\theta - (b_{22}-b_{11})\cos 2\theta. \tag{29}$$

Proposition 2 *If $q_4(\theta) \neq 0$, the solution of equation (28) is given by*

$$p(\theta) = \frac{K}{D(\theta)q_4(\theta)^2}(1 + \eta \int_0^\theta D(u)du), \tag{30}$$

where K is determined by the normality condition

$$\int_0^{2\pi} p(\theta)d\theta = 1, \tag{31}$$

and

$$\eta = \frac{D(2\pi) - 1}{\int_0^{2\pi} D(u)du}. \tag{32}$$

The function D is given by

$$D(\theta) = exp\Big(-2 \int_0^\theta \frac{q_3(u) - q_2(u)q_4(u) - q_4(u)q_5(u)}{q_4(u)^2}du\Big). \tag{33}$$

□

A numerical solution of the phase distribution could be performed by a simple backward difference scheme.

Let $N \in \mathbb{R}_+$ and $h = \frac{\pi}{N}$. Let

$$\begin{aligned}
q_1(i) &= a_{11}\cos^2(ih) + (a_{12} + a_{21})\cos(ih)\sin(ih) + a_{22}\sin^2(ih),\\
q_2(i) &= b_{11}\cos^2(ih) + (b_{12} + b_{21})\cos(ih)\sin(ih) + b_{22}\sin^2(ih),\\
q_3(i) &= a_{21}\cos^2(ih) + (a_{22} - a_{11})\cos(ih)\sin(ih) - a_{12}\sin^2(ih),\\
q_4(i) &= b_{21}\cos^2(ih) + (b_{22} - b_{11})\cos(ih)\sin(ih) - b_{12}\sin^2(ih),\\
q_5(i) &= -(b_{12} + b_{21})\sin(2ih) - (b_{22} - b_{11})\cos(2ih).
\end{aligned} \tag{34}$$

The $p(i)$, $i = 0, ..., N$ is given by the following relations

$$p(i) = (p(0) + \frac{q_4(i)^2 p(i-1)}{2h})F(i),$$

where

$$F(i) = \frac{2h}{2h(-q_3(i) + q_2(i)q_4(i) + q_4(i)q_5(i)) + q_4(i)^2}.$$

The Lyapunov function is $\lambda = \lambda(N)$, where

$$\lambda(N) = \sum_{i=1}^{N}(q_1(i) + \frac{1}{2}(q_4(i)^2 - q_2(i)^2))p(i)h.$$

Proposition 3 *If the matrix B is given by*

$$b_{11} = \alpha,\ b_{12} = -\beta,\ b_{21} = \beta,\ b_{22} = \alpha,$$

probability distribution $p(\theta)$ is given by

$$p(\theta) = \frac{K}{\beta^2} exp\{\frac{1}{\beta^2}((a_{21} - a_{12} - \alpha\beta)\theta + \frac{1}{2}(a_{11} - a_{22})\cos 2\theta + \frac{1}{2}(a_{21} - a_{12})\sin 2\theta\},$$

$$K = \frac{\beta^2}{\int_0^{2\pi} exp\{\frac{1}{\beta^2}((a_{21} - a_{12} - \alpha\beta)\theta + \frac{1}{2}(a_{11} - a_{22})\cos 2\theta + \frac{1}{2}(a_{21} - a_{12})\sin 2\theta\}} d\theta,$$

and the Lyapunov exponent is given by

$$\lambda = \frac{1}{2}(a_{11} + a_{22} + \beta^2 - \alpha^2) + \frac{1}{2}(a_{11} - a_{22})c_2 + \frac{1}{2}(a_{21} + a_{12})s_2,$$

where

$$c_2 = \int_0^{2\pi} \cos(2\theta)p(\theta)d\theta, \quad s_2 = \int_0^{2\pi} \sin(2\theta)p(\theta)d\theta.$$

□

A2 The Euler scheme.

In general 2-dimensional case, the Euler scheme has the form:

$$x_i(n+1) = x_i(n) + f_i(x(n))h + g_i(x(n))G_i(n),\ i = 1, 2, \tag{35}$$

with Wiener process increment

$$G_i(n) = W_i((n+1)h) - W_i(nh),\ n = 0, ..., N-1,\ i = 1, 2,$$

and $\xi(n) = \xi(nh, \omega)$, $G_i(n)$ are generated using boxmuller method.

It is shown that Euler scheme has the order for weak convergence 1, for sufficiently regular drift and diffusion coefficients.

We assume that f_i and g_i in (35) are sufficiently smooth such that the following schemas are well defined.

The second order Euler scheme is defined by the relations

$$\begin{aligned} x_i(n+1) &= x_i(n) + f_i(x(n))h + g_i(x(n))G_i(n) + g_i(x(n))\frac{\partial}{\partial x_i(n)}g_i(x(n))\frac{G_i(n)^2 - h}{2} + \\ &+ \Big[f_i(x(n))\frac{\partial f_i(x(n))}{\partial x_i(n)} + \frac{1}{2}(g_i(x(n))^2\frac{\partial^2 f_i(x(n))}{\partial x_i(n)\partial x_i(n)}\Big]\frac{h^2}{2} + \Big[g_i(x(n))\frac{\partial f_i(x(n))}{\partial x_i(n)} \\ &+ f_i(x(n))\frac{\partial g_i(x(n))}{\partial x_i(n)} + \frac{1}{2}(g_i(x(n))^2\frac{\partial^2 g_i(x(n))}{\partial x_i(n)\partial x_i(n)}\Big]\frac{hG_i(n)}{2},\ i = 1, 2, \end{aligned}$$

where we used the random variables $G_i(n)$, $i = 1, 2$. In [11], it is shown that these schemes converge weakly with order 2.

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